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MAIL STOP PCT  
Attorney Docket: 26797U

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

BRAUNGER, et al.

Serial No.: 10/542,088

Filed: July 13, 2005

Internatl. Appl. No.: PCT/EP04/00196

Internatl. Filing Date: 14 January 2004 (14.01.2004)

Title: PDE4 INHIBITORS FOR THE TREATMENT OF NEOPLASMS OF LYMPHOID CELLS

TRANSMITTAL LETTER

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

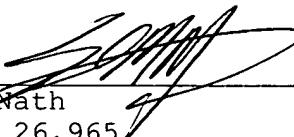
Submitted herewith for filing in the U.S. Patent and Trademark Office is the following:

- (1) Transmittal Letter;
- (2) Information Disclosure Statement;
- (3) PTO Form 1449 with 27 cited References;
- (4) Copies of 27 of the 27 cited References.

The Commissioner is hereby authorized to charge any deficiency or credit any excess to Deposit Account No. 14-0112.

Respectfully submitted,  
**NATH & ASSOCIATES PLLC**

Date: October 17, 2005

By:   
Gary M. Nath  
Reg. No. 26,965  
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GMN/SMM/iy (NP.IDS)

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Art Unit: Unknown

Examiner: Unknown

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INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

An Information Disclosure Statement is submitted herewith pursuant to 37 C.F.R. 1.97-1.98. Please note the following particulars: [NOTE: One only of items a, b, c, and d must be checked.]

[**XXX**] a. The enclosed statement is being filed within three months of the filing date of a national application, or within three months of the date of entry into the national stage as set forth in 37 C.F.R. 1.491 in an international application, or before the mailing date of a first Office Action on the merits, whichever event occurs last.

[ ] b. The enclosed statement is being filed after a first action on the merits but before the mailing date of a final action under 37 C.F.R. 1.113, or a notice of allowance under 37 C.F.R. 1.311.

The enclosed statement is accompanied by [check one]:

[ ] i. a certification in part (e) below as specified in 37 C.F.R. 1.97(e), or

[ ] ii. a check in the amount required by 37 C.F.R. 1.17(p).

[ ] c. The enclosed statement is being filed after the mailing date of a final action under 37 C.F.R. 1.113, or a notice of allowance under 37 C.F.R. 1.311, but before payment of the issue fee.

[ ] Certification report(e) below; and

[ ] a check in the amount as required by 1.17(p).

- [ ] d. The enclosed statement is being filed pursuant to 37 C.F.R. 1.97(i), for placement in the file.
- [ ] e. Certification [Check one] [Certification is required only if box (b)(i) or box (c) is checked.]
- [ ] I hereby certify that each item of information contained in the enclosed Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement,

or

- [ ] I hereby certify that no item of information in the enclosed Information Disclosure Statement herewith was cited in a communication from a foreign patent office in a counterpart foreign application, or, to my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

or

- [ ] Appropriate certification is attached.

- [XXX] f. If no check is enclosed and a fee is due in connection with this communication or if the check enclosed is insufficient, the Commissioner is authorized to charge any fee or additional fee due in connection with this communication to Deposit Account No. 14-0112.
- [XXX] g. Copies of the documents are attached herewith with a completed Form PTO-1449.

or

- [ ] Copies of the documents are not attached as allowed under CFR 1.98(d)(1)(2). The earlier application is identified as:

and/or

- [ ] Copies of US Patents/Publications not attached as allowed in Official Gazette Aug. 5, 2003/ Vol. 1273, no. 1.

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Attorney Docket: 26797U  
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The Examiner is respectfully requested to cite the documents listed on the attached Form PTO-1449 in the next Office Action. In so doing, the Examiner is respectfully requested to initial in the space adjacent to the listing of each document on the Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicants, to confirm that these documents have been considered by the Examiner and made of record in this application.

If the Examiner has any questions or wishes to discuss this application, kindly telephone the undersigned at the below-listed number.

Respectfully submitted,  
**NATH & ASSOCIATES PLLC**

Date: October 17, 2005

By:

  
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Reg. No. 26,965  
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| <b>FORM PTO-1449</b><br><b>INFORMATION DISCLOSURE<br/>CITATION</b> | Attorney Docket: 26797u                 | In re Application of:<br>Braunger, Schudt  |
|  | Group Art Unit: Unknown                 | Examiner: Unknown                          |
|  | Serial No.: 10/542,088                  | Filed: July 13, 2005                       |
|  | Internatl. Appl. No.:<br>PCT/EP04/00196 | Internatl. Filing Date:<br>14 January 2004 |

**FOREIGN PATENT DOCUMENTS**

| Examiner Initial | Document Number | Issued/Published Date | Country | Class | Sub-Class | Translation |
|------------------|-----------------|-----------------------|---------|-------|-----------|-------------|
| A1               | 1 188 438       | 20.03.02              | EP      |       |           | N/A         |
| A2               | 00/16621        | 30.03.00              | WO      |       |           | N/A         |
| A3               | 01/13953        | 01.03.01              | WO      |       |           | N/A         |
| A4               | 01/30777        | 03.05.01              | WO      |       |           | N/A         |
| A5               | 01/78651        | 25.10.01              | WO      |       |           | N/A         |
| A6               | 01/93909        | 13.12.01              | WO      |       |           | N/A         |
| A7               | 02/064584       | 22.08.02              | WO      |       |           | N/A         |
| A8               | 02/092064       | 21.11.02              | WO      |       |           | N/A         |
| A9               | 98/41232        | 24.09.98              | WO      |       |           | N/A         |
| A10              | 99/34804        | 15.07.99              | WO      |       |           | N/A         |
| A11              | 99/49859        | 07.10.99              | WO      |       |           | N/A         |

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| A12 | Jun Zhu et al. "How acute promyelocytic leukaemia revived arsenic", <u>Nature Reviews, Cancer</u> , vol. 2, pp. 705-713, (2002).   |
| A13 | Ryosuke Ogawa et al. "Inhibition of PDE4 phosphodiesterase activity induces growth suppression apoptosis, glucocorticoid sensitivity, p53, and p21 <sup>WAF1/CIP1</sup> proteins in human acute lymphoblastic leukemia cells", <u>Blood</u> , vol. 99, no. 9, pp. 3390-3397, (2002). |
| A14 | Martin S. Tallman, MD. "Differentiating therapy with all-trans retinoic acid in acute myeloid leukemia", <u>Leukemia</u> , Vol. 10, Supp. 1, pp. S12-S15, (1996).  |
| A15 | Peter Norman, "PDE4 inhibitors: sustained patenting activity as leading drugs near the market", <u>Exp. Opinion. Ther. Patents</u> , vol. 10, No. 9, pp.1415-1427, (2000)  |
| A16 | Peter Reid, "Rofluitlast", <u>Current Opinion in Investigational Drugs.</u> , vol. 3, No. 8, pp.1165-1170, (2002).   |
| A17 | David Raeburn et al. "Anti-inflammatory and bronchodilator properties of RP 73401, a novel and selective phosphodiesterase type IV inhibitor", <u>Br. J. Pharmacol.</u> , vol. 113, pp.1423-1431, (1994).  |
| A18 | Gary A. Piazza et al. "Exisulind, a Novel Proapoptotic Drug, Inhibits Rat Urinary Bladder Tumorigenesis", <u>Cancer Research</u> , vol. 61, pp. 3961-3968, (2001)  |
| A19 | B. Siegmud et al. "Phosphodiesterase type 4 inhibitor suppresses expression of anti-apoptotic members of the Bcl-2 family in B-CLL cells and induces caspase dependent apoptosis", <u>Leukemia</u> , vol 15, pp. 1564-1571, (2001).  |
| A20 | H. Kosugi et al. "Histone deacetylase inhibitors are the potent inducer/enhancer of differentiation in acute myeloid leukemia: a new approach to anti-leukemia therapy", <u>Leukemia</u> , vol. 13, pp. 1316-1324, (1999).   |
| A21 | Della Makower et al. "Therapeutic efficacy of theophylline in chronic lymphocytic leukemia", <u>Medical Oncology</u> , vol. 16, pp. 69-71, (1999).   |

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**OTHER** (Including Author, Title, Date, Pertinent Pages, etc.)

|    |   |
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| B1 | Frank Mentz et al. "Theophylline Synergizes With Chlorambucil in Inducing Apoptosis of B-Chronic Lymphocytic Leukemia Cells", <u>Blood</u> , vol. 88, No. 6, pp. 2172-2182, (1996).   |
| B2 | Frank Mentz et al. "Theophylline, a new inducer of apoptosis in B-CLL: role of cyclic nucleotides", <u>British Journal of Haematology</u> , vol. 90, pp. 957-959, (1995).   |
| B3 | Motasim Billah et al. "Synthesis and Profile of SCH351591, a Novel PDE4 Inhibitor", <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , vol. 12, pp. 1621-1623, (2002).   |
| B4 | Marie-Claude Guillemin et al. "In Vivo Activation of cAMP Signaling Induces Growth Arrest and Differentiation in Acute Promyelocytic Leukemia", <u>J. Exp. Med.</u> vol. 196, No. 10, pp. 1-9, (2002).  |
| B5 | L.A. Sorbera et al. "Roflumilast", <u>Drugs of the Future</u> , vol. 25, No. 12, pp. 1261-1264, (2000).   |
| B6 | Gregory J. Kato et al. "Growth of Acute Lymphoblastic Leukemia Cells Is Suppressed by $\beta$ -1 Adrenergic Agonists and the Novel Water Soluble Forskolin NKH477", <u>Pediatric Hematology</u> , John Hopkins University School of Medicine, Poster. 26, p. 1178 |

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|----------|-----------------|
| Examiner | Date Considered |
|----------|-----------------|

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP ' 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.